DOCKET NO.: ISIS-4682 Application No.: 09/775,967 Office Action Dated: May 27, 2004

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

REMARKS

Claims 1-6, 11-15, 21, 36-40, 47-52, 56-60, 66, 81-85, 92-101, 103, and 104 are pending. No claims are added, amended, or canceled.

Claims 1-6, 11-15, 21, 36-40, 47-52, 56-60, 66, 92-97, and 104 are rejected as allegedly obvious under 35 U.S.C. § 103(a) over Caruthers et al., *Proceedings of the 2nd International Symposium on Phosporous Chemistry Directed Towards Biology* (1987), 3-21 ("the Caruthers reference") in combination with Nurminen et al, *J. Chem. Soc., Perkin Trans* 2, 1999, 2551-2556 ("the Nurminen reference"). The Office Action alleges that the method taught by the Caruthers reference is the same as the instantly claimed method except for the identity of the neutralizing agent (page 4 of the Office Action). The Office Action further alleges that one skilled in the art would be motivated to combine the teaching of the Nurminen reference with the teaching of the Caruthers reference to arrive at the instantly claimed inventions (pages 4-6 of the Office Action). Applicants respectfully submit that both allegations are incorrect.

The instantly claimed process differs significantly from that of the Caruthers reference. Claim 1, for example, is directed to a process where the support bound oligomer has at least one *unprotected internucleoside linkage* selected from the group consisting of phosphate linkages, phosphorothioate linkages, and phosphorodithioate linkages. The process disclosed by Caruthers utilizes *protected phosphate linkages* which, as discussed on page 4, line 15 to page 5, line 22 of the filed specification, cause disadvantages versus the instantly claimed procedures. The Nurminen reference does not cure this defect. Thus, even if one were motivated to combine the teachings of the Nurminen reference with the Caruthers reference, the instant claims would not be obvious as the cited art does not teach all elements of the instant claims. The above argument applies equally to other claims which also stand rejected by the same arguments. As such, Applicants respectfully submit that the rejection is improper and should be withdrawn.

One skilled in the art would not be motivated to combine the teachings of the Nurminen reference with those of the Caruthers reference. As admitted in the Office Action, the Caruthers reference does not disclose the use of D⁺E⁻ neutralizing agents (page 4 of the Office Action). The Office seeks to remedy this deficiency by cited the Nurminen reference.

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The Nurminen reference, however, shows the use of certain neutralizing agents in the context of reacting diisopropylphosphonite with t-butyl alcohol while the instant invention, in contrast, uses D^+E^- neutralizing agents in the context of oligomer synthesis. While discussing DNA synthesis generally, the Nurminen reference does not show equivalent reactions for DNA synthesis. Thus, even if D^+E^- gives a faster rate of reaction in reaction of the Nurminen reference, it does not necessarily follow that the same effect would be found by using D^+E^- in the instant process. As such, one skilled in the art would lack sufficient motivation to select a particular neutralizing agent from the Nurminen reference and apply it to the process of the Caruthers reference. For at least this reason, Applicants request reconsideration and withdrawal of the rejection.

Claims 98-101, and 103 stand rejected as allegedly obvious over the Caruthers reference in combination with the Nurminen reference. For reasons entirely analogous to those discussed in the preceding paragraph, one skilled in art would not be motivated to combine the teachings of the Caruthers reference and the Nurminen reference. As such, Applicants respectfully request reconsideration and withdrawal of the rejection.

Applicants submit that all of the claims presently before the Examiner patentably define the invention over the prior art and are otherwise in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,

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